REMARKS

This is a reply to the Final Office Action of December 15, 2000 and is being submitted with a Request for Continued Examination. Claims 1, 2, 3, 21 and 22 have been cancelled. Claims 4 and 17 have been amended to more clearly and specifically describe Applicants' invention. New claims 31-34 have also been added. Support for these amendments to the claims and the new claims may be found throughout the Specification. No new matter has been added. A marked up copy of the claims, with bracketing and underlining to denote additions and deletions, respectively accompanies this submission.

A. Summary of the Invention

Applicants' invention relates to the field of nucleic acid sequence analysis. Specifically, the invention provides methods of nucleic acid sequence analysis that use combinatorial sequence array primers to sequence and/or to detect mutations or polymorphisms within a template nucleic acid. Sequencing and/or detection are accomplished by determining a region of complementarity by use of a sequencing reagent that contains a primer and extending that primer in order to determine whether there was complementarity.

B. Summary of the Amendment

Claims 1 –3 and 21 –22 have been canceled. Claims 29 and 30 were the non-elected claims for which the Applicants have not yet requested prosecution. However, Applicants reserve the right to prosecute them at a later time. Thus, claims 4 –20, 23 – 28 and 31 –34 are currently under consideration.

Claim 4 has been rewritten in independent form and more precisely defines the sequencing reagent that is used in Applicants' pending claims. Specifically, amended claim 4 describes a method that uses a sequencing reagent in which the spacer region is adjacent to the primer region and during the scanning step, there is no hybridization of the spacer to the

template molecule. Support for these amendments may, for example, be found on page 15 and 16 of the Specification.

Claim 17 has been amended to define the size of the spacer in nanometers. Support for this amendment may be found on page 15 of the Specification.

New claims 31 –34 have been added. Claim 31 is dependent on claim 27 and describes a method wherein the detection by change in mass is through mass spectrometry. Support for this claim may be found on page 29 of the Specification.

Claim 32 is dependent on claim 4 and describes the repetition of the methods of claim 4 so that a pattern of signals for the template may be generated. Support for this claim may be found on pages 22 – 24 of the Specification.

Claim 33 is dependent of on claim 4 and describes a method that uses a sequencing reagent that contains a primer region of between 4 and 6 bases. Support for this may be found on page 16 of the Specification.

Claim 34 is dependent on claim 4 and describes a method that uses a sequencing reagent in which the capture moiety is bound to the spacer and the spacer is located between the capture moiety and the primer region. Support for this may be found on page 16 of the Specification.

C. Responses to Office Action dated December 15, 2000

1. The Failure to Comply With 37 C.F.R. § 1.821 (a)(1) and (a)(2)

In the Office Action dated December 15, 2000, the Examiner contends that the application failed to comply with the requirements of 37 C.F.R. §1.821 through §1.825 because no submission of computer readable form sequences had been submitted. A copy of the Sequence Listing in computer readable form on a 3.5 inch diskette is enclosed herewith. Applicants note that they submitted a Sequence Listing in computer readable form on a 3.5 inch diskette with their response that was submitted on September 25, 2000, but it appears that there was a technical problem with the diskette. For the Examiner's convenience,

Applicants enclose herewith an additional paper copy of the Sequence Listing. The paper copy of the Sequence Listing and Computer readable copy of the initial Sequence Listing are identical and meet the requirements of 37 C.F.R. §§1.821 –1.825. Therefore, Applicants respectfully submit that the enclosed Sequence Listing fully satisfies the requirements of 37 C.F.R. §§1.821 –1.825. In view of the foregoing amendment, the enclosed substitute Sequence Listing and diskette, it is respectfully submitted that this objection is obviated.

2. The Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected Claim 2 under 35 U.S.C. §112, second paragraph as being indefinite. Applicants have cancelled Claim 2 and submit that a response to this rejection is no longer necessary.

3. The Rejection Under 35 U.S.C. § 102(e)

The Examiner rejected Claims 1 – 27 in light of the U.S. Patent No. 5,795,714 (the "Cantor patent"). Applicants provided a synopsis of the Cantor patent in their response dated September 25, 2000 and will not repeat that synopsis herein. Instead, Applicants will briefly explain why the Cantor Patent does not anticipate the pending claims as amended. Applicants respectfully disagree with the Examiner's conclusions in the December 15, 2000 Final Office Action, but in the interest of furthering prosecution have amended their claims.

Applicants have cancelled claims 1 –3 and 21 –22 and will not address the rejections as applied to those claims.

The Examiner asserted that Applicants' then pending claim 4 was anticipated by the Cantor reference. In Applicants' response dated September 25, 2000, Applicants noted that the capture, spacer and primer regions were distinct units. The Examiner responded "these units are characterization of segments of a hybridizable segment as utilized in Cantor et al. without any distinction in instant claim 4 as to what distinguishes these moieties from a hybridizable segment as utilized in Cantor et al. which may arbitrarily be called capture, spacer, or primer region of a somewhat lengthy nucleotide sequence." Applicants have amended claim 4 to more precisely define a method that uses a reagent in which the primer, the spacer and the capture region are defined as distinct units. For example, in the method of

amended claim 4 the spacer is not capable of hybridizing to regions of the template adjacent to a region complementary to the primer. Thus, Applicants respectfully submit that the Cantor Patent does not anticipate, teach, disclose or otherwise suggest claim 4 as amended.

Pending claims 5-20, 23- 27, as well and new claims 31 –34 are dependent on claim 4. Because claim 4 is not anticipated or otherwise taught, disclosed or suggested by the Cantor Patent, these dependent claims are also not anticipated or otherwise taught, disclosed or suggested by the Cantor Patent.

4. Rejection under 35 U.S.C. § 103

The Examiner rejected claims 1-28 as being unpatentable over the Cantor patent in view of Pease, *et al.* (the "Pease reference"). As discussed above, Applicants have cancelled claims 1-3 and 21 –22 and applicants submit that Cantor patent does not anticipate, teach, disclose or otherwise suggest pending claims 4-20, 23- 28 and 31 – 34. The missing elements described above would not be obvious to one skilled in the art. Thus, because the Cantor patent fails to teach, to disclose or to suggest elements of each of these claims, it does not render these claims obvious.

Further, Applicants respectfully disagrees with the Examiner's position that the Pease reference discloses the limitations missing from the Cantor patent and request that the Examiner reconsider Applicants' arguments in their September 25, 2000 response, as well as his position in light of the amendments above and remove the rejection under 35 U.S.C. § 103.

CONCLUSION

For the reasons set forth above, it is submitted that the claims of the subject application are patentable over the art of record considered alone or in any combination. Early allowance of the application is therefore earnestly solicited.

If any additional fees are determined to be necessary or any overpayment has been made, please charge or credit our Deposit Account No. 11-0171 as appropriate.

Respectfully submitted,

by: _____

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Boyce-Jacino et al

Examiner: Marschel, A.

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Assistant Commissioner for Patents
Washington, DC 20231

MARKED UP CLAIMS IN ACCORDANCE WITH 37 CFR §1.121(c)

Dear Sir:

REMARKS

In accordance with 37 CFR §1.121 (c) the following marked up claims are submitted herewith to accompany the amendment filed concurrently for the application identified above.

4. (Amended) A [The] method for analyzing a sequence of a template, said method [of Claim 3 wherein the array is an array of sequence reagents, each sequence reagent] comprising:

   (a) capturing the template with a sequencing reagent to form a captured template, said sequencing reagent comprising:

      i. a capture moiety;

ii. a spacer region [moiety]; and

iii. a primer region, wherein said primer region is adjacent to said spacer region;

(b) forming a primer-polymerase complex, said primer-polymerase complex comprising said primer region and a polymerase;

(c) scanning the captured template using said primer-polymerase complex for a region of complementarity to said primer region wherein said region of complementarity to said primer region is not adjacent to a region that is complementary to said spacer region;

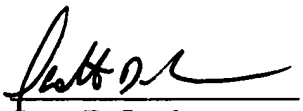
(d) extending the primer by at least two nucleotide moieties by means of a template-homology dependent extension reaction to form an extended primer; and

(e) detecting said extended primer,

wherein detecting said extended primer indicates the presence of one or more regions of complementarity to the primer in the captured template.

17. (Amended) The method according to [of] Claim 4 wherein the spacer region is at least 10 nm [Å] in length.

Respectfully submitted,



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